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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,528	01/29/2004	Karl Salzwedel	1900.0430002/LBB/SJE	2237

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,528	SALZWEDEL ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10, 12, 13, 82-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,13 and 82-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/19/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 28 August 2006. Claims 11 and 14-81 have been cancelled. Claims 82-84 are newly added and read on the invention in Group I.

Election/Restriction

Applicant elects Group I, claims 1-10, 11, 12, and 82-84, with traverse. The traversal is on the grounds that there is no search burden in examining the different Groups of Inventions together. Applicant's traversal is unpersuasive because, as indicated in the prior Office Action, there are different limitations in each Group that require a separate search. While a search of the prior art for one Group may overlap with that of another group, the searches are not co-extensive and thus would be an undue burden on Office resources.

Information Disclosure Statement

An initialed and dated copy of each of Applicant's IDS form 1449, filed on 19 August 2004, is attached to the instant Office action.

Double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 12, 13, and 82-84 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 19, 21, 22, 24, and 25 of copending Application No. 10/766,528. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims anticipated by the copending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, 1st ¶, written description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12, 13, and 82-84 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the

application was filed, had possession of the claimed invention. This is a written description rejection.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical*

properties, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

M.P.E.P. § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." M.P.E.P. § 2163 also states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See M.P.E.P. § 2163. Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are directed to a method of treating HIV-1 infection in a patient, comprising administering to a patient a compound that selectively inhibits processing of the viral Gag p25 protein (CA-SP1) to p24 (CA). The scope of the

invention encompasses all compounds and functional derivatives or homologs that inhibit processing of viral Gag p25. Thus, the claims are drawn to a genus of compounds that is defined only by a functional characteristic.

The specification only provides description for one compound, 3-O-(3',3'-dimethylsuccinyl) betulinic acid (DSB). See spec. ¶26, and examples. There is no disclosed correlation between function and structure beyond the DSB disclosed in the examples in the specification. Neither does the specification identify any partial structure that must be conserved for inhibition of viral Gag p25 processing. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus.

As discussed above, the skilled artisan cannot envision the detailed chemical structure and function of the encompassed genus of compounds. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or synthesis.

While having written description of *** identified in the specification examples, the specification is devoid of any other compounds that qualify for the functional characteristics claimed. A definition by function alone "does not suffice, to sufficiently describe a coding sequence" because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119F.3 at 1568, 43USPQ2d at 1406.

Therefore, claims 1-10, 12, 13, and 82-84 do not meet the written description provision of 35 U.S.C. §112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variable. Applicant is reminded

that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (page 1115).

Claim Rejections - 35 USC § 112, 1st ¶, enablement

Claims 1-10, 12, 13, and 82-84 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors (MPEP §2164.01(a)).

Nature of the invention. The claims are drawn to a method of treating HIV-1 infection in a patient, comprising administering to a patient in need thereof a compound that selectively inhibits processing of the viral Gag p25 protein (CA-SP1) to p24 (CA).

State of the prior art. At the time the invention was made, successful implementation of HIV/AIDS therapy with a Gag p25 inhibitor was not routinely obtainable by those skilled in the art.

Breadth of the claims. The broad claims encompass treatment of all clades and subtypes of HIV in a patient.

Working examples. The working examples disclose *in vitro* inhibition of HIV infection in Hela cells.

Guidance in the specification. The specification provides no guidance regarding practice of the claimed method. The amount of direction is limited to a cell culture assay to determine the inhibitory effect of DSB on HIV maturation (spec. pages

53-54, Example 3, ¶159). There is no evidence that shows any correlation with *in vivo* efficacy. There is not even a test to determine the cytopathic effect and resistance of the claimed genus of Gag p25 inhibitors. *In vitro* testing is, at most, useful tool for screening potential anti-viral agents but is not predictive of *in vivo* effectiveness. *Ex parte Balzarini* (BdPat App&Int) 21 USPQ2d 1892. One skilled in the art would not associate successful *in vitro* testing results with successful *in vivo* AIDS treatment due to the high level of unpredictability of this art.

Predictability of the art. The state of the art of development of pharmaceutical HIV inhibitors is highly unpredictable, since HIV replicates rapidly with a high mutational frequency and creates diverse 'quasi-species', which are favored by the Darwinian selective pressures. Therefore, efforts to develop effective treatments and vaccines must overcome the complex evolutionary dynamics in HIV-infected individuals and within affected populations. Besides the problem of rapid emergence of drug-resistance HIV variants, the disclosed *in vitro* test is unreliable in detecting the drug susceptibility of minority HIV-1 variants in the virus population because resistant mutants may not persist at detectable levels in the absence of drug selection pressure (Martinez-Picado, 1998, pages 84, 85, and 87), which increases the complexity in extrapolating from *in vitro* to *in vivo* test results. For determining in vivo efficacy, one skilled in the art has to address many factors such as serum half-life, bioavailability, clearance of the drugs themselves (Gait, 1995, page 437), cellular uptake, transport, metabolic activation, cell-, tissue-, and organ-specific toxicity (Lee, 2003, page 14713), all of which affect the concentration of the active form of the drugs at the site of action. Due to the highly

unpredictable nature of HIV-infection, extrapolating from *in vitro* models to whole organisms without *in vivo* validation is hazardous and unpredictable.

Amount of experimentation necessary. Absent working examples and specific teachings of the efficacy in humans, therapeutic index, and pharmacokinetic properties of the Gag p25 inhibitors, those in the art would not be able to use the claimed method for the treatment of HIV infection. One skilled in the art is burden with the undue experimentation of clinical efficacy, therapeutic index, and pharmacokinetic properties of the genus of Gag p25 inhibitors because one can use the claimed method. Applicants have identified a candidate compound, DSB, that affects HIV maturation, but essentially all of the work required to ultimately develop a treatment method has been left for others.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Remarks

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP §714.02 and §2163.06.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
14 September 2006

9/14/06